REMARKS

This Amendment is submitted in response to the December 27, 2000 Office Action issued in connection with the subject application. Reconsideration and reexamination are respectfully requested in view of the above amendments and the remarks below.

By this Amendment, applicants have amended the punctuation of claim 11 for clarification purposes in response to the Examiner's rejection of said claim under 35 USC 112, second paragraph. The amendments to claim 11 do not change the scope of the claim and therefore do not raise an issue of new matter.

The Examiner also kindly noted that references to Figures 6D, 7D, 8D, 9D, and 12C are missing from the "Brief Description of the Figures" section of the specification. This was clearly due to an inadvertent error, and it is clear from the Figures that 6D, 7D, 8D, 9D, and 12C were part of Figures 6, 7, 8, 9, and 12, respectively, as a whole. The specification has been amended herein accordingly, and applicants maintain that since it is clear as to what Figures 6D, 7D, 8D, 9D, and 12C belong, such amendment does not raise an issue of new matter.

Accordingly, since the amendments herein do not raise an issue of new matter, applicants request that the amendments herein be entered.

It is also noted that a Notice of Draftsperson's Patent Drawing Review objecting to the Drawings of the Figures *per se* of the subject application accompanied the December 27, 2000 Office Action. Applicants presume they are not required to attend to correcting the Drawings until the subject application is deemed otherwise allowable.

Rejections under 35 USC 112, Second Paragraph

In the December 27, 2000 Office Action, the Examiner alleged that claims 1-3, 11, 13, and 16 are indefinite for supposedly failing to particularly point out and distinctly claim the subject matter regarded as the invention.

According to the Examiner, claims 1-3, 13 and 16 comprise an element that encompasses any endogenously synthesized peptide, and this element is allegedly not enabled "by the scope of the claimed invention".

Applicants respectfully traverse this rejection. The Examiner's rejection is made under 35 USC 112, second paragraph. Applicants assert that the "endogenously synthesized peptide" term of claims 1-3, 13 and 16 does indeed particularly point out and distinctly claim the subject matter regarded as the invention. The term "endogenously-synthesized peptide" is defined, for example, at page 10, lines 20-23 of the specification. The specification states that "endogenously-synthesized peptide" means a peptide that is synthesized by a vertebrate as part of the vertebrate's metabolic functioning and that examples of endogenously-synthesized peptides include, but are not limited to, hormones and enzymes. Some examples of specific endogenously-synthesized peptides (e.g. GnRH, IgE, cand cholecystokinen) are described in the specification at page 15, lines 1-21. Based on this description in the specification, it is clear what qualifies as an endogenously-synthesized peptide and what falls within the realm of the present claims accordingly.

The Examiner also rejected claim 11, asserting that portions (a) and (b) of the recited fusion protein seem to be reversed in claim 11 relative the fusion protein claimed in claim 1. The Examiner seems to be of the impression that in

claim 11, proteinaceous portion (a)is derived to protect against infection by a pathogen and portion (b) is the endogenously synthesized protein. This is not what applicants intended in claim 11, and it seems clear in current claim 11 that portion (a) still refers to the endogenously synthesized peptide and portion (b) still refers to an immunogen from a pathogen. Claim 11 states recites inhibition of the activity of the peptide from which portion (a) of the fusion protein is derived (emphasis added) and protection against infection by the pathogen from which portion (b) of the fusion protein is derived (emphasis added). Nonetheless, applicants have amended claim 11 herein to clarify the claim language; in particular, applicants have added Roman numerals (I) and (II) to identify the two requirements that must be met for the amount of fusion protein, vector or transformed cell in the claimed vaccine to be an "effective amount". Applicants have also deleted from claim 11 "in a vertebrate which endogenously synthesizes the peptide and which can be pathogenically infected by the pathogen", since this clause is simply superfluous to the rest of the claim language. This clause is superfluous since it is understood that the inhibition of activity of the peptide must occur in a vertebrate that endogenously synthesizes the peptide, and since protection against infection by the pathogen from which proteinaceous portion (b) is derived must be with respect to protecting a vertebrate which can be pathogenically infected by said pathogen. Thus, deletion of the clause "in a vertebrate which endogenously synthesizes the peptide and which can be pathogenically infected by the pathogen" does not change the scope of claim 11 and merely simplifies claim 11.

The Examiner also indicated that she is confused by the language "the fusion protein is derived in a vertebrate which

endogenously synthesizes the peptide which can be pathogenically infected by the pathogen" in claim 11. It is not clear to applicants where in claim 11 the Examiner is extrapolating the aforementioned clause. It is believed that the comments in the aforementioned paragraph and the amendments herein to claim 11 should help clarify claim 11 to the Examiner. As further explanation: claim 11 is directed to a dual-function vaccine that can comprise either a fusion protein (as recited in claim 1), a vector encoding the fusion protein, or a transformed cell expressing the fusion protein. The vaccine claimed in claim 11 is a "dual-function" vaccine because it provides an inhibitory immune response in a vertebrate to two different things: a) it inhibits the activity of a peptide that the vertebrate endogenously synthesizes, and b) it protects the vertebrate from infection by a pathogen to which the vertebrate is susceptible. Thus, the vaccine has a "dual-function", i.e. it functions in two ways: a) inhibiting the activity of an endogenously synthesized peptide, and b) protecting against infection by a pathogen. In order to achieve these two functions, the vaccine must comprise an amount of the fusion protein, vector, or transformed cell that is both effective in inhibiting the activity of the peptide and effective in protecting against infection by the pathogen. This is clarified in the new claim 11 provided herewith.

In view of the above, applicants respectfully request that the Examiner reconsider and withdraw the rejections made under 35 USC 112, second paragraph.

Rejection Under 35 USC 103

In the December 27, 2000 Office Action, the Examiner rejected claims 1-17 under Van Der Zee et al. (U.S. Patent 5,684,145) in view of Mittal et al. The Examiner stated that

the claims of the subject application are directed to a fusion protein producing a dual immune response in a vertebrate that comprises a first proteinaceous portion that is GnRH, and that the activity of the GnRH is to be inhibited in the vertebrate. The second portion of the fusion protein is, according to the Examiner, an immunogenic gD from BHV-1. The Examiner stated that a dual-function vaccine that comprises the fusion protein inhibits the activity of endogenous GnRH, which includes inhibiting the sexual characteristics in a cow, and protects against BHV-1.

According to the Examiner, Van Der Zee et al. teaches a recombinant DNA molecule that codes for a hybrid protein comprising GnRH that is conjugated top e. coli fimbrial-filiments in a vaccine and elicits an immune response against GnRH. The Examiner stated that the recombinant DNA molecule is expressed in a microorganism and that a microorganism is equivalent in the art to a host cell. The Examiner stated that previous attempts to completely elicit an immune response against GnRH have been unsuccessful due to the fact that GnRH itself is non-immunogenic and therefore needs a strong immunogenic carrier to elicit an effective immune response against GnRH, such as E. coli fimbrial-filiments that have strong antigenic properties. The Examiner notes that in Example 3, adult rats that were given the plasmid containing the hybrid protein showed serum antibody binding, which showed a disruption and suppression of estrous cycles. The Examiner stated that bulls that were immunized with the plasmid resulted in a reduction of scrotal growth compared to control animals. The Examiner stated that Van Der Zee et al. does not teach using gD from BHV-1 as the immunogenic component to the fusion protein.

The Examiner stated that Mittal et al. teaches that a full-length recombinant form (gD) and a truncated form of gD (tgD) from BHV-1 was inserted into a human adenovirus type 5 vector. According to the Examiner, the antigenicity of both proteins was found to be similar to native gD expressed in BHV-1 infected cells. The Examiner stated that the vaccine resonse in animals was better using the full-length form (gD) than tgD. The Examiner stated that furthermore, after vaccine challenge, no infectious BHV-1 virions were isolated from the rats previously immunized with the full-length gD.

In the Examiner's view, one of ordinary skill in the art would have been motivated to combine the "strong immunogenicity of gD", allegedly taught by Mittal et al., with successful evokation of a complete immune response against GnRH when expressed with a "strongly antigenic carrier", allegedly taught in Van Der Zee et al., in order to both 1) suppress the endogenous hormone, and 2) protect against disease. The Examiner stated that from the references one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention because Van Der Zee et al. supposedly indicates that all that is needed to induce an immune response against GnRH is a strong immunogenic carrier, which is what gD from BHV-1 is supposedly from Mittal et al. The Examiner concluded that applicants' claimed invention is therefore as a whole *prima facie* obvious.

Applicants respectfully traverse the aforementioned obviousness rejection of claims 1-17 over Van Der Zee et al. in view of Mittal et al. Applicants submit that the Examiner's rejection is improperly based on hindsight. Nothing in either Van Der Zee et al. or Mittal et al. suggests the use of a carrier to protect against disease (in addition to promoting an immune response against the protein with which it is combined).

Thus, the allegation that one would have been motivated to combine GnRH with gD to "both 1) suppress the endogenous hormone, and 2) protect against disease" is pure hindsight and is improper.

Moreover, there is nothing in Mittal et al. that even suggests that BHV-1 gD could be used as a carrier. The Examiner stated that it was known that GnRH should be combined with a carrier of some sort if one wished to elicit an immune response against it (see, e.g. , Van Der Zee et al.). Thus, there would have been no motivation based on Van Der Zee et al. and Mittal et al. to combine BHV-1 gD with GnRH , since BHV-1 gD was not known or suggested in Mittal et al. to be useful as an immunogenic carrier.

In conclusion, applicants maintain that the claims of the subject application are not obvious and, as amended herein, particularly point out and distinctly claims the subject matter regarded as the invention.

If a telephone interview would be of assistance in advancing the prosecution of this application, the Examiner is kindly invited to telephone applicants' undersigned attorney at the telephone number provided.

No fee is believed necessary in connection with the filing of this Amendment, other than the fee for the three month extension of time authorized in the Petition filed herewith. However, if any other fee is found necessary in connection with filing this Amendment, authorization is hereby given to charge such fee to Deposit Account No. 16-1445.

Date: June 27, 2001

Respectfully submitted,

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APPENDIX A

Attorney Docket Number PC10202A

U.S. Serial No. 09/506,078

VERSION WITH MARKINGS TO SHOW CHANGES - DO NOT ENTER:

The claims of the above-indicated patent application are amended in the Amendment in response to the December 27, 2000 Office Action, to which this Appendix A is attached as follows:

In the Claims:

Claim 11 is amended as follows:

11. (Once Amended) A dual-function vaccine which comprises a fusion protein according to claim 1, a vector according to claim 7, or a transformed cell according to claim 10, in an amount effective to I) inhibit the activity of the peptide from which portion (a) of the fusion protein is derived, and II) to protect against infection by the pathogen from which portion (b) of the fusion protein is derived; and ~~in a vertebrate which endogenously synthesizes the peptide and which can be pathogenically infected by the pathogen, along with~~ a carrier acceptable for pharmaceutical or veterinary use.

APPENDIX B

Attorney Docket Number PC10202A

U.S. Serial No. 09/506,078

VERSION WITH MARKINGS TO SHOW CHANGES - DO NOT ENTER:

The specification of the above-indicated patent application is amended in the Amendment in response to the December 27, 2000 Office Action, to which this Appendix B is attached as follows:

In the Specification:

Paragraphs on page 6, lines 6-29, are amended as follows:

FIGURE 6: (Fig.6A-~~6C~~6D): pQE-tmgD. Nucleotide coding sequence for the tmgD, flanked by plasmid pQE-31 sequences, including a sequence encoding a 6XHIS tag, which is expressed connected to the tmgD (SEQ ID NO: 20). The amino acid sequence of the tmgD with the connected 6XHIS tag is also shown (SEQ ID NO: 21).

FIGURE 7 (Fig.7A-~~7C~~7D): Nucleotide coding sequence and flanking sequences for plasmid pQE-GnRH:gD (SEQ ID NO: 22). Amino acid sequence of the 4GnRH-tmgD fusion protein, including a 6XHIS tag, is also shown (SEQ ID NO: 23).

FIGURE 8 (Fig.8A-~~8C~~8D): pQE-gD:GnRH. Nucleotide coding sequence and plasmid flanking sequences are shown (SEQ ID NO: 24). The amino acid sequence of the tmgD-4GnRH, with a 6XHIS tag, is also shown (SEQ ID NO: 25).

FIGURE 9 (Fig.9A-~~9C~~9D): pQE-GnRH:gD:GnRH. Nucleotide coding sequence and plasmid flanking sequences are shown (SEQ ID NO: 26). The amino acid sequence of the 4GnRH-tmgD-4GnRH, with a 6XHIS tag, is also shown (SEQ ID NO: 27).

FIGURE 10: Comparison of expression products from bacterial vector pQE constructs. " A" is pQE-tmgD, " B" is pQE-gD:GnRH, " C" is pQE-GnRH:gD, and " D" is pQE-GnRH:gD:GnRH. The amino acids which link the gD portions, the GnRH tetramers, and the 6XHIS tags are depicted in this figure.

FIGURE 11 (Fig. 11A-11B): Nucleotide sequence (SEQ ID NO: 28) from plasmid pCMV-tgD encoding a truncated gD, and deduced amino acid

sequence (SEQ ID NO: 29) of the truncated gD expression product including the signal sequence.

FIGURE 12 (Fig. 12A-~~12B~~12C): Nucleotide sequence (SEQ ID NO: 30) from plasmid pCMV-gD:GnRH (ATCC Accession No. 203370) encoding a tgD-4GnRH fusion protein, with deduced amino acid sequence (SEQ ID NO: 31) of the fusion protein product including signal sequence.